UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/295,925	04/21/99	JOSHI	P 16303-007510

020350 HM12/0410
TOWNSEND AND TOWNSEND AND CREW LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO CA 94111

EXAMINER	
WOITACH, J	
ART UNIT	**PAPER NUMBER**
1632	10

DATE MAILED: 04/10/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/295,925	Applicant(s) Joshi et al.
	Examiner Joseph Woitach	Group Art Unit 1632

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 MW month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-45* is/are pending in the application.

Of the above, claim(s) *13-45* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-12* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

Applicant's election of Group I in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 13-45 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cells sensitive to the effects of electromagnetic radiation, does not reasonably provide enablement for all cells. Further, while being enabling for x-ray radiation, the specification does not reasonably provide enablement for the whole spectrum of electromagnetic radiation. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

It is known in the art that chemical compounds which disrupt essential elements which affect cell cycle control and electromagnetic radiation that alter the DNA of a cell, such as x-ray and γ-ray radiation, will cause the cell to stop cycling at specific cell cycle check points until either the chemical is removed or the damaged DNA is repaired. Applicants demonstrate that cell cycle synchronization by chemical means can increase the efficiency of transformation and then by association the conclusion is made that x-rays increase the efficiency for similar reasons, i.e. cell cycle synchronization. While it has been established in the art that cells can be sensitive to certain types of electromagnetic radiation, there are many transformed cells which have acquired genetic alterations which make them insensitive to the effects of radiation and other cell synchronizing agents. For example, Vogelstein *et al.* describe p21-deficient cells which are defective in cell cycle check-point control and can not be synchronized by common agents, including radiation (figure 2c, figures 3i and 3k). Such transformed cells would not be altered by radiation and therefore, the efficiency of transformation would not be affected by the method recited in the claims. Thus the method is limited to cells which are sensitive to electromagnetic radiation.

In the specification only one example is presented where x-rays are used to examine the increase in the efficiency of transformation *in vivo* (figure 13 and pages 54-55; section 11), however, the example does not demonstrate that in this case the cells were synchronized by the x-rays only that there is an increase in efficiency of DNA taken-up by the cell. Further, there is no

example nor guidance in the specification that support the effect or ability of other forms of radiation, such as visible light and lower wave lengths, to affect the cell cycle of a cell. Since the mechanism for electromagnetic radiation for cell cycle synchronization is not described in the specification or the art on record, even if the cell cycle control of a cell is sensitive to certain types of electromagnetic radiation, such as x-ray radiation which cause DNA strand breaks and physically affect the DNA in the cell, one can not assume an inherent ability of all electromagnetic radiation to regulate the cell cycle in a similar manner. Also, there is no guidance nor examples which demonstrate that the cell can be synchronized with x-rays in any other state than G2/M, and so in claims 3, 4 and 5, it is unclear how a source of electromagnetic radiation can synchronize the cell at different points in the cell cycle.

In view of the of the lack of guidance, working examples, breadth of the claims, skill in the art and state of the art at the time of the claimed invention, it would require undue experimentation by one of skill in the art to practice the full scope of the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 1 is unclear in the recitation of 'transformation' because it is not clear if the radiation causes the cell to become transformed from a normal cell to a cancerous cell or if it is in reference to introducing a nucleic acid.

Claims 7, 8 and 9 are unclear in the recitation of 'said therapeutic gene' because there is not an antecedent basis and so it is not clear what is the gene or what is the genes therapeutic effect.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yorifuji *et al.* in view of Spang-Thomsen *et al.*

Yorifuji *et al.* teach that the cell cycle phase of cells affects the ability of the cell to be transformed with exogenous DNA, in particular that synchronized cells demonstrate a higher transformation efficiency when they are in S andG2/M phase of the cell cycle (page 202-203; figures 1 and 2). Further, Yorifuji *et al.* use the thymidine kinase gene, a foreign to the transformed cells, which is toxic to said cells when cultured in the appropriate conditions. Yorifuji *et al.* conclude that G2/M phase is the most efficient period for transformation (page 203; bridging paragraph of column 1 and 2). However, they do not teach use of electromagnetic radiation to synchronize the cells. Spang-Thomsen *et al.* teach that cells can be synchronized with different amounts of x-ray radiation (page 852; figure 2 and summarized in discussion). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to synchronize the cells as taught by Spang-Thomsen *et al.* in order to increase the efficiency of stable gene transfer as observed by Yorifuji *et al.* One having ordinary skill in the art would have been motivated to use electromagnetic radiation in order to avoid the need or complicating effects of chemicals to simplify the method of synchronization. There would have been a reasonable expectation of success given the results that different methods of synchronization were effective in increasing the transformation efficiency and thus cell cycle dependent (page 203; second column) suggesting that any form of synchronization would be effective including the x-ray radiation taught by Spang-Thomsen *et al.*

Thus, the claimed invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yorifuji *et al.* in view of Spang-Thomsen *et al.* as applied to claims 1-9, 11 and 12 above, and further in view of Lechardeur *et al.*

As discussed above, Yorifuji *et al.* in view of Spang-Thomsen *et al.* teach a method to synchronize cells with electromagnetic radiation to increase the efficiency of transformation with exogenous DNA, however they do not teach to transform the cell with a lipid-nucleic acid particle. Son *et al.* teach how to transform a cell with lipid-nucleic acid particle (page 12669; bottom of second column). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to transform the synchronized cells as taught by Spang-Yorifuji *et al.* in view of Thomsen *et al.* with the method taught in Son *et al.* One having ordinary skill in the art would have been motivated to use lipid-nucleic acid particles to simplify the method of transfection and to make it applicable to cells which may be sensitive to transformation by electroporation. There would have been a reasonable expectation of success given the results of Son *et al.* that the method of transformation which uses the lipid-nucleic acid particle could be used for synchronized cell cultures.

Thus, the claimed invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach, whose telephone number is (703) 305-3732. The examiner can normally be reached on Monday through Friday from 8:00 to 4:30 (Eastern time).

If attempts to reach the examine by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached on (703) 308-2035. The fax number for group 1600 is 1(703)308-4242.

An inquiry of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is (703) 308-0196.

Joseph T. Woitach

Bruce Campell

BRUCE R. CAMPELL
PRIMARY EXAMINER
GROUP 1800